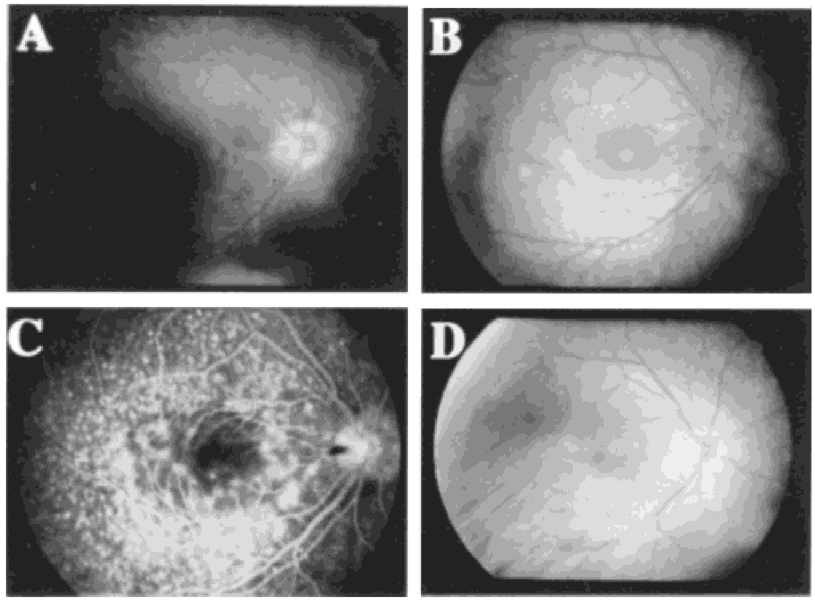

Fig. 1. Ophthalmoscopic findings of the right fundus. A: Blot retinal hemorrhages at first visit. B: Infiltration of leukemia cells into the choroid and resultant serous retinal detachment (before radiation therapy). C: Fluorescein angiography of right fundus before radiation therapy. Myriad diffuse leakage of dye was seen. D: Improvement of choroidal infiltration (after radiation therapy).

the blasts demonstrated: CD13(+), CD33(+), CD34(+), CD7(−), CD10(−), CD14(−), CD19(−). Chromosomal analysis of bone marrow leukemia cells showed karyotype abnormality: t(8;21) and loss of sex chromosome: −X. Therefore, she was finally diagnosed as AML-M2 according to the criteria of the French-American-British Cooperative Group classification (FAB), complicated by retinal hemorrhage. She attained a complete remission and all treatments were finished in October 1992. In September 1994, she suddenly presented a visual disturbance of the right eye. Ophthalmologic examination revealed choroidal infiltration of leukemia cells and infiltration-induced serous retinal detachment in the right eye. There was no evidence of CNS leukemia. Local radiation therapy improved her ophthalmologic findings (Fig. 1) and completely resolved her visual disturbance after receiving 30 Gy at the end of December 1994. In November 1994, we could not detect leukemia cells in the bone marrow using fluorescence *in situ* hybridization (FISH). Moreover, no leukemia cells in the bone marrow were detected by morphological examination and Southern blot analysis using the *AML1* probe in April 1995. She was last seen in complete remission in July 1995. However, she finally had bone marrow relapse in September 1995.

Although there was no histopathologic evidence for the direct infiltration of leukemia cells into the choroid, the visual disturbance in our patient was probably caused by choroidal infiltration of leukemia cells, given the ophthalmologic findings and the rapid therapeutic response to the local irradiation alone. So, we hypothesized that the initial retinal hemorrhage allowed ocular seeding of leukemia cells that became apparent 2 years after remission induction. Since frequency of ocular involvement in AML patients with retinal hemorrhage has not been reported, we could not conclude that there was a close relation between ocular involvement of AML and a history of retinal hemorrhage. Because there have been 13 (8.5%) cases of orbital involvement in 154 primary (or isolated) extramedullary leukemias [3], it may be necessary to irradiate for ocular prophylaxis in AML patients with a history of retinal hemorrhage during active disease in spite of organ toxicity of ocular irradiation.

In conclusion, local irradiation of ocular prophylaxis might be considered in AML patients, especially FAB-M2 and M4 subtypes [4], with retinal hemorrhage that contains leukemic cells. Frequency of ocular infiltration in patients with AML complicated by retinal hemorrhage and the efficacy of local irradiation for ocular prophylaxis in these patients must be studied.

Kimiharu Uozumi
Yoshifusa Takatsuka
Nobuhito Ohno
Shuichi Hanada
Yoshiaki Tabata
Hitoshi Arimura
Kumiko Nakao
Terukatsu Arima
Second Department of Internal Medicine, Faculty of Medicine, Kagoshima University, Kagoshima, Japan
Department of Ophthalmology, Faculty of Medicine, Kagoshima University, Kagoshima, Japan

References

1. Byrd JC, Weiss RB: Recurrent granulocytic sarcoma. An unusual variation of acute myelogenous leukemia associated with 8;21 chromosomal translocation and blast expression of the neural cell adhesion molecule. Cancer 73:2107–2112, 1994.
2. Meis JM, Butler JJ, Osborne BM, Manning JT: Granulocytic sarcoma in nonleukemic patients. Cancer 58:2697–2709, 1986.
3. Byrd JC, Edenfield WJ, Shields DJ, Dawson NA: Extramedullary myeloid cell tumors in acute nonlymphocytic leukemia: A clinical review. J Clin Oncol 13: 1800–1816, 1995.
4. Leonardy NJ, Rupani M, Dent G, Klintworth GK: Analysis of 135 autopsy eyes for ocular involvement in leukemia. Am J Ophthalmol 109:436–444, 1990.

Therapy-Related Acute Myeloid Leukemia With Minimal Myeloid Differentiation (AML-M0) Associated With a t(11;19)(q23;p13.3) Translocation

To the Editor: Chromosomal translocations affecting band 11q23 and the *MLL* gene rearrangement are strongly associated with therapy-related acute myeloid leukemia (t-AML) after treatment with epipodophyllotoxin. Most cases of epipodophyllotoxin-induced t-AML are classified as FAB subtype

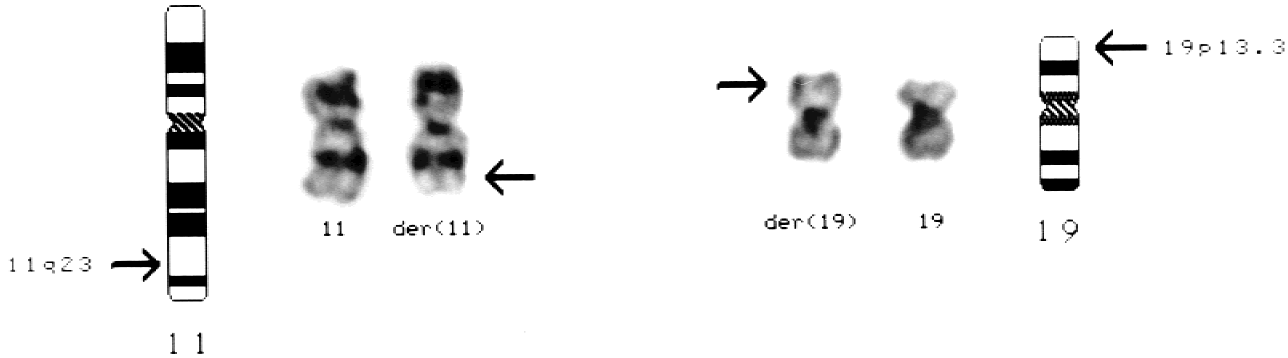

Fig. 1. Partial karyotype of the patient, showing t(11;19)(q23;p13.3), as revealed by G-banding technique. Breakpoints in the affected chromosomes are indicated by arrows.

M4 or M5 [1–3], with the M0 phenotype rarely observed. We now describe an adult patient with t-AML-M0 associated with t(11;19)(q23;p13.3) and *MLL* gene rearrangement that developed subsequent to epipodophyllotoxin therapy.

A 73-year-old Japanese man was diagnosed with unresectable stage IIIB small-cell carcinoma of the lung (SCLC) at the Kyushu Cancer Center in August 1992. The patient received four courses of EVAC-PE therapy (etoposide, vincristine, doxorubicin, cyclophosphamide, and cisplatin) and achieved partial remission. A low dose of etoposide was administered orally as maintenance therapy until December 1994 (cumulative dose of etoposide, 10,800 mg/m^2), at which time the SCLC remained in partial remission. In February 1995, the patient was admitted because of anemia, bleeding tendency, and pneumonia. Peripheral blood examination revealed Hb 8.2 g/dl, a platelet count of 26×10^9/l, and a white blood cell count of 3.2×10^9/l, with 51% blasts. Bone-marrow analysis detected 84.4% blasts, which were negative for both myeloperoxidase activity and staining with antibodies to myeloperoxidase. Mononucular cells in the bone marrow were positive for HLA-DR, CD33, and CD11c, and negative for CD2, CD3, CD5, CD7, CD10, CD19, CD22, and CD34. Accordingly, the patient was diagnosed with t-AML-M0. Cytogenetic analysis showed a karyotype of 46,XY,t(11;19)(q23;p13.3) in all 20 bone-marrow cells examined (Fig. 1). Southern blot analysis demonstrated a rearrangement of the *MLL* gene (data not shown). Chemotherapy with behenoylcytosine arabinoside (BHAC), daunorubicin, and prednisolone was initiated, and the number of leukemic blasts subsequently decreased. In March 1995, the number of leukemic blasts again increased, and the patient was treated with granulocyte colony-stimulating factor combined with a low dose of subcutaneous cytosine arabinoside. Despite additional chemotherapy with BHAC, aclarubicin (ACR), and very low-dose ACR, remission was not achieved. The patient died of pulmonary infection 3 months after presentation. Autopsy showed that the SCLC was in a state of complete remission.

Only three cases of t-AML-M0 associated with epipodophyllotoxin treatment have previously been described [1,2]. Although chromosome rearrangements affecting band 11q23 were apparent in all 3 individuals, cytogenetic abnormalities involving this band are rarely associated with de novo AML-M0 [4].

t(11;19) translocations have been detected not only in childhood acute lymphoblastic leukemia and leukemias with monoblastic differentiation, but also in adult patients with AML expressing lymphoid-associated markers. Whereas t(11;19)(q23;p13.3) is predominant in younger individuals with lymphoid, biphenotypic, or congenital myeloid leukemia, t(11;19)(q23;p13.1) is frequently associated with both de novo and therapy-related AML, usually of the M4 or M5 phenotype, in patients of all ages [5]. Thus, translocations affecting region 19p13.3 tend to be associated with a more immature phenotype of leukemia than those involving 19p13.1.

We have described a rare case of adult t-AML-M0 that was associated with t(11;19)(q23;p13.3) and induced by treatment of SCLC with etoposide. The involvement of chromosome band 19p13.3 possibly contributed to the immature phenotype (M0) of the leukemia in this patient.

Acknowledgments

We thank K. Kuriyama for anti-myeloperoxidase antibody staining.

Youko Suehiro
Naokuni Uike
Midori Kumagawa
Tatsuro Goto
Koichiro Muta
Mitsuo Kozuru

Department of Hematology, National Kyushu Cancer Center Hospital, Fukuoka, Japan

References

1. Pui C-H, Relling MV, Rivera GK, Hancock ML, Raimondi SC, Heslop HE, Santana VM, Ribeiro RC, Sandlund JT, Mahmoud MH, Evans WE, Crist WM, Krance RA: Epipodophyllotoxin-related acute myeloid leukemia: A study of 35 cases. Leukemia 9:1990, 1995.
2. Pui C-H, Ribeiro RC, Hancock ML, Rivera GK, Evans WE, Raimondi SC, Head DR, Behm FG, Mahmoud MH, Sandlund JT, Crist WM: Acute myeloid leukemia in children treated with epipodophyllotoxins for acute lymphoblastic leukemia. N Engl J Med 325:1682, 1991.
3. Hunger SP, Tkachuk DC, Amylon MD, Link MP, Carroll AJ, Welborn JL, Willman CL, Cleary ML: HRX involvement in de novo and secondary leukemias with diverse chromosome 11q23 abnormalities. Blood 81:3197, 1993.
4. Cuneo A, Ferrant A, Michaux J-L, Boogaerts M, Demuynck H, Van Orshoven A, Criel A, Stul M, Dal Cin P, Hernandez J, Chatelain B, Doyen C, Louwagie A, Castolodi G, Cassiman J-J, Van Den Berghe H: Cytogenetic profile of minimally differentiated (FAB M0) acute myeloid leukemia: Correlation with clinicobiologic findings. Blood 85:3688, 1995.
5. Huret JL, Brizard A, Slater R, Charrin C, Bertheas MF, Guilhot F, Hahlen K, Kroes W, Van Leewen E, Schoot EVD, Beishuizen A, Tanzer J, Hangemeijer A: Cytogenetic heterogeneity in t(11;19) acute leukemia: Clinical, hematological and cytogenetic analyses of 48 patients—Updated published cases and 16 new observations. Leukemia 7:152, 1993.

Hypofibrinogenemia Induced by Prednisolone Therapy in a Patient With Chronic Lymphocytic Leukemia Complicated With Autoimmune Hemolytic Anemia

To the Editor: We report on the first instance of hypofibrinogenemia caused by sole administration of prednisolone (PSL).

In August 1992, a 54-year-old male developed antiglobulin test-positive autoimmune hemolytic anemia (AIHA) secondary to chronic lymphocytic leukemia (CLL) which had not been treated. He was given PSL (1 mg/kg/